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Models for Transmission and Control of Bioterroristic Epidemics

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Models for Transmission and Control of Bioterroristic Epidemics

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Abstract

A deterministic model for control of a bioterrorist epidemic in a large nonhomogeneous population is presented. Primary considerations in model development are the representation of a large nonhomogeneous population of individuals and the implementation of the model for quick numerical execution. The model represents the effect of mass pre-vaccination and mass vaccination during the epidemic. It is recognized that the vaccination can result in life threatening complications. The model also represents the effect of tracing and quarantining as control options. The model has been implemented in Java for a Web-based educational tool. Numerical examples (pp. 12-15) illustrate possible behavior of populations exposed to such a disease as smallpox. Various disease controls such as vaccination and case tracing are studied.

1. Background, Overview, and Emphasis

For several years, especially since the Twin Towers and anthrax attacks, bioterrorist acts such as deliberate epidemic initiation have been recognized as possible serious threats to the U.S. homeland and to allies. Consequently, studies have been

initiated and pursued of (Red—bioterrorist) initiation, propagation, and possible (Blue) detection, identification, and control.

There are many scientific articles on Red bioterrorist opportunities and possible CONOPS, and on the effect of various Blue detection and control strategies: methods of detection, identification, and interruption of the cumulative effects of a virulent and destructive epidemic. This paper describes mathematical models for Red attacks and Blue attempts to achieve control. The paper by Kaplan, Craft, and Wein (2002) espoused mass vaccination. A recent monograph, H. T. Banks and C. Castillo-Chavez (2003), (denoted B&C), is a useful introduction to the field; the reference listing of this paper provides further background, but is not totally comprehensive. The present presentation (G&J, 2004) has the objective of broadening and extending models and approaches like those in B&C, and elsewhere. Like the latter, we concentrate on characterization of epidemics, emphasizing the effects of:

- *Nonhomogeneous mixing* of infectious with susceptible individuals;
- Vaccination effects and efficacy (and risks) as a control option for Blue;
- Tracing and isolation (quarantining) as a control option for Blue;
- Value of *information* to Blue in attempting to thwart terrorist endeavors to create true epidemics (or pseudo-epidemics introduced for low-cost deception as “decoys”). Value and use of intelligence information and/or *syndromic surveillance*;
- Counter-Bioterrorism as a Command-and-Control (C4ISR) problem;
- The (Blue) resource requirements for detection, prevention, and mitigation/treatment of disease epidemics, possibly a combination of different

types, some intended to disable security forces guarding water, electricity, transportation, and financial assets.

The approach of this paper is to create simple mathematical models for various situations, here deterministic or “fluid” (but stochastic-probabilistic, or a combination to appear later), *and to use these models to provide “user-friendly” graphical/numerical tools for the use of health-care professionals, administrators, and other decision makers whose training and concerns are primarily practical and action-oriented, NOT primarily highly technical/mathematical.* We aim to provide the basis and beginning of a transparent tool to build insight.

To the above end we first:

- Emphasize *discrete-time* (e.g., daily time-step) difference-equation formulations rather than continuous-time classical differential equations, as in B&C and earlier.
- Formulate deterministic models for an epidemic in a large nonhomogeneous population of individuals that can be implemented for quick numerical execution.

2. A Deterministic/“Fluid” Model for Disease Transmission and Control

Suppose there are \bar{H} individual and effectively isolated households or families. Assume temporarily and for simplicity that all households contain the same initial number of individuals, N . In this model an infected individual from any household can infect individuals in other households that have no infected individuals by interacting in the exterior world, that is a “marketplace,” transportation system, or even hospital or airport. We assume that the probability that several individuals within a household are

infected from outside the household is very small, and can be neglected (this can be generalized). When a household is newly infected, it has one infectious individual; other individuals in the household with the infectious person cannot be infected by others outside the household; the susceptible individuals in the household with an infectious individual are infected by infectious individuals within the household according to, for example, the classical S-I-R model of Kermack and McKendrick (Daley and Gani (1999) p. 28, also Banks and Castillo-Chavez (2003, Chapter 2)). Of course, other within-household epidemic models are possible, but are not treated here. Once an individual in a household has been infected, we can describe the subsequent spread of the disease within the household with the classical S-I-R epidemic model.

2.1 Continuous-Time Model for the Within-Household Epidemic

Let

$f(i;t)$ be the mean number of individuals infectious at time t in a household (or family);

$f(s;t)$ be the mean number of individuals susceptible at time t in a household;

$f(r;t)$ be the mean number of individuals removed (no longer infectious because of recovery or death) at time t in a household; once an individual is removed, the individual becomes immune: never becomes susceptible or infected again.

The conventional differential equations for evolution of the disease in a representative household are as follows:

$$\begin{aligned}\frac{d}{dt}f(i;t) &= \lambda f(i;t)f(s;t) - \mu f(i;t) \\ \frac{d}{dt}f(s;t) &= -\lambda f(i;t)f(s;t) \\ \frac{d}{dt}f(r;t) &= \mu f(i;t)\end{aligned}\tag{2.1a}$$

with $f(i;0)=1$, $f(s;0)=N-1$, $f(r;0)=0$. The parameters λ and μ are per-unit infection and recovery rates (here assumed constant, although they may realistically vary with time and environment, a realistic feature that can and should be considered in subsequent work.

2.2 A Discrete-Time Model for the Within-Household Epidemic

A discrete-time model for the evolution of the disease within a particular household is as follows; time steps can be in days. Let p_I be the probability that a susceptible individual is infected by an infectious individual within a household during one (arbitrary, but fixed) time period; let p_R be the probability that an infectious individual can no longer infect others, either because he/she recovers during such a time period, or dies. In the equations below

$F(i;t)$ is the mean number of infectious individuals in the household at time t ;

$F(s;t)$ is the mean number of susceptible individuals in the household at time t ;

$F(r;t)$ is the mean number of individuals that were at one time infectious, but can no longer infect others in the household at time t ; and

$$\begin{aligned} F(i;t+1) &= F(i;t)[1-p_R] + F(s;t)\left[1-(1-p_I)^{F(i;t)}\right] \\ F(s;t+1) &= F(s;t)\left[(1-p_I)^{F(i;t)}\right] \\ F(r;t+1) &= F(r;t) + F(i;t)p_R \end{aligned} \quad (2.1b)$$

As before, $F(i;0)=1$; $F(s;0)=N-1$; $F(r;0)=0$, although other initial conditions are also possible; the mean time an individual is contagious is $1/p_R$.

2.3 The Two-Level Model

We call this type of epidemic model a *compound model* or *two-level model*. The two-level epidemic model reduces to a classical homogeneous mixing epidemic model if there is only one (large) household; this thus resembles the model of Kaplan, Craft, and Wein (2002). With more than one household, the disease is spread between households by homogeneous mixing. We assume that at most one individual in a household will be infected by an infectious individual from outside the household; that is, the chance of more than one individual within a household being infected by a person outside the household, i.e., in the “marketplace,” is negligible. The spread of the disease within a household with at least one infectious individual is governed by the homogenous mixing epidemic model within that household (omitting those household members that have been removed). This two-level epidemic model is most representative of diseases that are more likely to be spread among close individual contacts, (household or family members), than distant individual contacts, (outside of household or family). Ball and Lyne (2002) also use households to represent population nonhomogeneity.

Individuals can be vaccinated; for the present, we assume the vaccination is *perfect*: 100% effective with no latency period. When a household is vaccinated, all members of the household are vaccinated. Some of the households may be pre-vaccinated before the outbreak of the disease. Let H be the number of households whose members are all susceptible at the time the epidemic starts; these households have not been pre-vaccinated. The time until a household is vaccinated has an exponential distribution with mean V/H where V is the level of vaccination resource per time period, and H is the number of households that have not been pre-vaccinated; all individuals in a household

are vaccinated effectively simultaneously, on one visit by a vaccinator. Let time be measured discretely, say in terms of days. *We will establish the convention that vaccination and tracing occur at the beginning of a day before individuals are possibly exposed to infectious individuals*; other conventions are possible. State values are nonnegative real numbers.

Fluid State Definitions

$\tilde{I}(0;t)$ be the mean total number of *infectious individuals* at time t in households that have *not been vaccinated*.

$\tilde{R}(0;t)$ be the mean total number of individuals that have *been infectious*, but are no longer infectious at time t in households whose *individuals have not been vaccinated*.

$\tilde{S}(0;t)$ be the mean total number of individuals that are *susceptible* at time t in households whose individuals have *not been vaccinated*.

$\tilde{I}(v;t)$ be the mean total number of *infectious individuals* in households whose individuals have *been vaccinated* at time t .

$\tilde{R}(v;t)$ be the mean total number of individuals that *have been infectious*, but are *no longer infectious* in households that *have been vaccinated* at time t .

$\tilde{S}(v;t)$ be the mean total number of individuals that were *susceptible* in households whose members *have been vaccinated* by time t .

\bar{H} be the total number of households.

H be the number of households that have not been pre-vaccinated.

$H_v(0;t)$ be the mean number of households *vaccinated* by time t that never contained any infected individuals.

$H_v(1;u;t)$ be the mean number of households *vaccinated* by time t that acquired their first infected individual at time $u < t$.

$H(0;t)$ be the mean number of households continually without infection and not vaccinated during $(0,t]$.

$H(1;u;t)$ be the mean number of households whose members *have not been vaccinated* by time t and acquired their first infected individual at time $u < t$.

$H_f(1;u;t)$ be the mean number of households whose members are *not vaccinated* that acquired their first infected individual at time $u < t$ and *are traced or identified* by time t .

When a household is traced or identified, all the members of the household are removed from the population (isolated or quarantined) and no more susceptible members in the household are infected. An individual can be traced/identified by interviewing contacts of individuals who are known to have the disease. An individual can also be traced/identified if the individual seeks out health care because of media coverage that the disease is present. In the equations below, we adopt the convention that individuals are vaccinated and/or traced before being exposed to infectious individuals during a time period; other conventions are possible. Note that we are approximating the probability that a new household is vaccinated by not updating the number of households that have not been vaccinated at each time.

$$H_v(0;t+1) = H_v(0;t) + H(0;t) \left[1 - e^{-V/H} \right] \quad (2.2)$$

$$H_v(1;u;t+1) = H_v(1;u;t) + H(1;u;t) \left[1 - e^{-V/H} \right] \quad (2.3)$$

$$H(0;t+1) = H(0;t) \exp \left\{ -\lambda_o \frac{g(i;t+1)}{\bar{H} \times N} \right\} e^{-V/H} \quad (2.4)$$

Where $g(i;t)$ is the mean number of infected individuals in households that have not been traced at time t including those in vaccinated households; these individuals can infect individuals in households with no infected individuals; λ_o is the rate of infection of a member of a uninfected household by an outside infectious individual.

A household with at least one infected individual can be traced. Let B be the effort expended for tracing; B may be the result of advertising the outbreak of the disease and encouraging individuals that think they have been exposed to seek help. Let p_T be the conditional probability that a household with an infectious individual is recognized as such by tracing; the household is then assumed to be immediately removed from the population (quarantined). We establish the convention that a household is traced before it may be exposed to susceptible people. The mean number of households that are not vaccinated, were infected at time $u < t$, and are traced during $(0, t+1]$ is

$$H_f(1;u;t+1) = H_f(1;u;t) + H(1;u;t)e^{-V/H} \left[1 - \exp\left\{-\frac{B}{H}\right\} \right] p_T. \quad (2.5)$$

The number of households at time $t+1$ with its first individual infected at time $u < t$ that have not been vaccinated or traced is

$$H(1;u;t+1) = H(1;u;t)e^{-V/H} \left[\exp\left\{-\frac{B}{H}\right\} + \left[1 - \exp\left\{-\frac{B}{H}\right\} \right] [1 - p_T] \right]. \quad (2.6)$$

The mean number of households vaccinated at time t that acquired their first infected individual at time $u < t$ is

$$h_v(1;u;t) = H_v(1;u;t) - H_v(1;u;t-1) \quad (2.7)$$

for $u = 0, 1, 2, \dots, t-1$.

If the continuous-time within-household epidemic (2.1a) is being used, and in the following $f(i, t + 1 - u)$ is the solution of (2.1a), evaluated at integer time points, we write

$$g(i; t + 1) = \sum_{u=0}^t \underbrace{H(1; u; t)}_{\substack{\text{number} \\ \text{households} \\ \text{that have not} \\ \text{been vaccinated} \\ \text{with 1st infected} \\ \text{at time } u}} f(i; t + 1 - u) + \sum_{w=0}^{t+1} \sum_{u=0}^w \underbrace{h_v(1; u; w)}_{\substack{\text{number} \\ \text{households} \\ \text{vaccinated at} \\ \text{time } w \\ \text{with 1st infected} \\ \text{at time } u < w}} f(i; w - u) \underbrace{e^{-\mu(t+1-w)}}_{\substack{\text{prob.} \\ \text{individ.} \\ \text{still} \\ \text{infected}}}, \quad (2.8a)$$

where $1/\mu$ is the mean time until an infectious individual stops being infectious; another model option is to quarantine all infectious people in a household. If the discrete-time epidemic model (2.1b) is used then

$$g(i; t + 1) = \sum_{u=0}^t \underbrace{H(1; u; t)}_{\substack{\text{number} \\ \text{households} \\ \text{that have not} \\ \text{been vaccinated} \\ \text{with 1st infected} \\ \text{at time } u}} F(i; t + 1 - u) + \sum_{w=0}^{t+1} \sum_{u=0}^w \underbrace{h_v(1; u; w)}_{\substack{\text{number} \\ \text{households} \\ \text{vaccinated at} \\ \text{time } w \\ \text{with 1st infected} \\ \text{at time } u < w}} F(i; w - u) \underbrace{[1 - p_R]^{t+1-w}}_{\substack{\text{prob.} \\ \text{individ.} \\ \text{still} \\ \text{infected}}} \quad (2.8b)$$

$$H(1; t + 1, t + 1) = H(0; t) \left[1 - \exp \left\{ -\lambda_o \frac{g(i; t + 1)}{\bar{H} \times N} \right\} \right] e^{-V/H}. \quad (2.9)$$

If all infectious individuals are quarantined when a household is vaccinated, then the mean number of infected individuals that can infect others outside the household is

$$g_0(i; t + 1) = \sum_{u=0}^t \underbrace{H(1; u; t)}_{\substack{\text{number} \\ \text{households} \\ \text{that are not vaccinated} \\ \text{with 1st infected} \\ \text{at time } u}} f(i; t + 1 - u). \quad (2.10)$$

In this case,

$$H(1; t + 1, t + 1) = H(0; t) \left[1 - \exp \left\{ -\lambda_o \frac{g_0(i; t + 1)}{\bar{H} \times N} \right\} \right] e^{-V/H}. \quad (2.11)$$

If the continuous-time within-household epidemic model (2.1a) is used, then

$$\begin{aligned}
\tilde{I}(0;t+1) &= \sum_{u=0}^{t+1} H(1;u;t+1) f(i;t+1-u) \\
\tilde{S}(0;t+1) &= \sum_{u=0}^{t+1} H(1;u;t+1) f(s;t+1-u) + H(0;t+1)N. \\
\tilde{R}(0;t+1) &= \sum_{u=0}^{t+1} H(1;u;t+1) f(r;t+1-u)
\end{aligned} \tag{2.12}$$

Similar equations result if the discrete-time epidemic model (2.1b) is used.

If the continuous-time within-household epidemic model (2.1a) is used, then

$$\begin{aligned}
\tilde{I}(v;t+1) &= \sum_{w=0}^{t+1} \sum_{u=0}^w h_v(1;u;w) f(i;w-u) e^{-\mu(t+1-w)} \\
\tilde{S}(v;t+1) &= \sum_{w=0}^{t+1} \sum_{u=0}^w h_v(1;u;w) f(s;w-u) \\
\tilde{R}(v;t+1) &= \sum_{w=0}^{t+1} \sum_{u=0}^w h_v(1;u;w) \left[f(i;w-u) \left[1 - e^{-\mu(t+1-w)} \right] + f(r;w-u) \right]
\end{aligned} \tag{2.13a}$$

If the discrete-time within-household epidemic model (2.1b) is used, then

$$\begin{aligned}
\tilde{I}(v;t+1) &= \sum_{w=0}^{t+1} \sum_{u=0}^w h_v(1;u;w) F(i;w-u) [1-p_R]^{t+1-w} \\
\tilde{S}(v;t+1) &= \sum_{w=0}^{t+1} \sum_{u=0}^w h_v(1;u;w) F(s;w-u) \\
\tilde{R}(v;t+1) &= \sum_{w=0}^{t+1} \sum_{u=0}^w h_v(1;u;w) \left[F(i;w-u) [1-[1-p_R]^{t+1-w}] + F(r;w-u) \right]
\end{aligned} \tag{2.13b}$$

When the continuous-time epidemic model (2.1a) is used, the number of individuals infected by the disease in $(0,t]$ that will be killed by the disease is

$$\begin{aligned}
K(d;t) &= [\tilde{I}(0;t) + \tilde{R}(0;t)]\kappa(d) \\
&+ \sum_{w=0}^t \sum_{u=0}^w h_v(1;u;w) [f(i;w-u)[1-\kappa(v)]\kappa(d) + f(r;w-u)[1-\kappa(v)]\kappa(d)], \quad (2.14) \\
&+ \sum_{u=0}^t H_f(1;u;t) [f(i;t-u) + f(r;t-u)]\kappa(d)
\end{aligned}$$

where $\kappa(d)$ is the probability an infected individual is killed by the disease and $\kappa(v)$ is the probability an individual is killed by the vaccine; a similar equation results if the discrete-time epidemic model (2.1b) is used. The mean number of individuals killed by vaccination is

$$\begin{aligned}
K(v;t) &= \sum_{w=0}^t \sum_{u=0}^w h_v(1;u;w) N\kappa(v) \\
&+ H_v(0;t) N\kappa(v)
\end{aligned} \quad (2.15)$$

3. Numerical Examples

Example 1: Disease is spread mainly through close contacts and the vaccination has life-threatening side effects. Smallpox is often spread through respiratory droplets; e.g., by an infectious individual coughing near one or more of the susceptibles. Most of the secondary cases are family members and healthcare workers. The average number of secondary cases per infected individual is here assumed to be 3.5 to 6. The fatality rate is about 30% in unvaccinated individuals. There is a vaccine for smallpox. The vaccine can have life-threatening complications; one estimate for death due to complications of the vaccine in the civilian population is the probability of 1.1×10^{-6} for people vaccinated for the first time (Center for Infectious Disease Research and Policy Web site, University of Minnesota: <http://www.cidrap.umn.edu/cidrap/content/bt/smallpox/biofacts/smlpx-summary.html>).

In the model, whose results appear below, there are 2×10^6 households. Each household has 5 members. An individual that is infectious with smallpox displays visible symptoms and so we assume that the mean time a diseased individual is infectious is 2 days before the person is quarantined. We use the continuous-time within-household epidemic model (2.1a) evaluated at integer times to represent the within-household progression of the disease. The daily rate at which an infected individual infects a susceptible in an all-susceptible household outside his/her household is $\lambda_0 = 0.03$; the rate at which a infectious individual infects a susceptible within his/her own family is $\lambda = 0.03$; with this infection rate, and one infected individual at time 0, the mean number of infected individuals within the household at time 50 is 4 with no intervention. The probability that an individual dies from the disease is 0.3. The probability with which a vaccinated individual dies from the vaccine is 1.1×10^{-6} . When a household is vaccinated all infectious members of the household are removed from the population (quarantined); all susceptible individuals are vaccinated and become either immune or die from vaccination. Traced households with infectious individuals are assumed here to be identified as such with probability 1. Initially, there are 100 households; each with 1 individual infected at time 0. The Table 1 displays model results at time 50 days.

Table 1

Disease is spread mainly through close contacts and has a large probability of mortality.
The vaccine has a substantial probability of life-threatening side effects.

Percentage pre-vaccinated	Vaccination resource: V per day	Tracing resource: B per day	Mean number individuals that are or were infected	Mean number of individuals killed by disease	Mean number of individuals killed by vaccination
0	0	0	427	128	0
0	0	100,000	257	77	0
0	100,000	0	255	77	10
20%	0	0	417	127	2
20%	100,000	0	235	71	11

Discussion: Individuals with this disease mainly infect those in the same household. The disease tends not to be transmitted to individuals outside of a household. As a result, tracing of households with infectious individuals is the most effective procedure to decrease the number of disease plus vaccination-caused fatalities; (pre-vaccination and vaccination in combination result in the smallest mean number killed by disease, but increase the number killed by vaccination). The probability of death due to vaccination is small; however, if many individuals are vaccinated, then deaths due to vaccination can be greater than the lives saved by vaccination.

Example 2: The disease considered here is relatively easily spread outside of a household and is rarely fatal. The vaccine has few serious side effects.

There are 2×10^6 households. Each household has 5 members. The mean time a diseased individual is infectious is 2 days. The rate at which an infected individual infects someone outside his/her household is $\lambda_0 = 0.5$; the rate at which an infectious individual infects a susceptible within his/her own family is $\lambda = 0.5$. The probability that an individual dies from the disease is 0.07. The probability with which a vaccinated individual dies from the vaccine is 10^{-7} . When a household is vaccinated, all infectious

members of the household are removed from the population (quarantined); all susceptible individuals either become immune, or die from vaccination. Traced households with infectious members are identified correctly with probability 1. Initially, there are 100 infected individuals at time 0; each one is in a different household. Table 2 displays model results at time 50 days.

Table 2

Disease spread through close and distant contacts. The vaccine has a small probability of life-threatening side effects.

Percentage pre-vaccinated	Vaccination resource: V per day	Tracing resource: B per day	Mean number individuals that are or were infected	Mean number of individuals killed by disease	Mean number of individuals killed by vaccination
0	0	0	4,250	305	0
0	0	10,000	2,043	143	0
0	10,000	0	1,105	77	1
20%	0	0	1,886	132	0
20%	10,000	0	832	58	1

Discussion: The most effective disease control procedure is pre-vaccination and continuing vaccination. Vaccination alone without pre-vaccination results in almost 50% more infected individuals than vaccination with pre-vaccination. Tracing is not as effective as vaccination since it cannot isolate households before the disease is transmitted to individuals outside the household. However, it does reduce the number killed by disease by about one-half of those that die with no preventive treatment. The vaccine has few life-threatening side effects. Vaccination results in 1 additional fatality.

4. Conclusions and Further Work

The above model has been implemented in Java by R. Simons and G. Bullock; Bullock and Simons (2004). The Java applet uses the discrete-time within-household epidemic model (2.1b). The model gives plausible comparisons of the effects of

controlling an outbreak of a disease by vaccination and tracing. Parameter values can be inserted and the resulting changes in the numbers of individuals in different states observed via the software GUI.

Many generalizations and modifications can be made to the deterministic model. A few of them are: generalize the within-household epidemic model to include latency and other disease characteristics; modify the representation of vaccination to include a time until the vaccinated person is immune to the disease, and the vaccine is less than 100% effective; introduce an initial time until the existence of the disease outbreak is known; represent a special category of people consisting of first responders and health-care workers and their families. Many other enhancements are possible.

It is also important to develop stochastic models for control of epidemics in large populations that can be implemented for rapid numerical execution. Stochastic models would provide insight to decision makers concerning the robustness of control policies. Thus it is recommended that stochastic models, especially those that represent environmental variations through the transmission parameters (so-called “doubly stochastic” (Cox and Isham (1980))) be developed in subsequent work.

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